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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/003,211	10/31/2001	Jeffrey L. Browning	A013 US CON	6970

7590 09/10/2004

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EXAMINER	
YAEN, CHRISTOPHER H	

ART UNIT	PAPER NUMBER
1642	

DATE MAILED: 09/10/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/003,211	BROWNING ET AL.	
	Examiner	Art Unit	
	Christopher H Yaen	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *31 October 2001*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *51-58* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *51-58* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *10/31/01*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

RE: Browning J. *et al*
Priority Date: 25 October 1996

1. The amendment filed 10/31/2001 is acknowledged and entered into the record. Accordingly, claims 1-50 are canceled without prejudice or disclaimer, claims 51-58 are newly added.

2. Claims 51-58 are pending and examined on the merits.

Information Disclosure Statement

3. The Information Disclosure Statement filed 10/31/2001 is acknowledged and considered. A signed copy of the IDS is attached hereto.

Claim Rejections - 35 USC § 112, 1st paragraph

4. Claims 51-58 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The written description in this case only sets forth a method of treating systemic lupus erythematosus (SLE) comprising the administration of a soluble lymphotoxin beta receptor (sLTβR) of SEQ ID NO:1 (as shown in Fig. 1) conjugated to an immunoglobulin Fc domain and therefore the written description is not commensurate in scope with the claims which read on the broad class of sLTβR or to the numerous heterologous proteins to which the sLTβR molecule is to be conjugated.

Vas-Cath Inc. V. Mahurkar, 19 USPQ2d 1111, clearly states that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention*. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed*." (See page 1117). The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (*See Vas-Cath* at page 1116).

Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 USC 112 is severable from its enablement provision (see page 115).

For the purposes of this rejection the claims are read to the extent that sLTβR encompasses fragments of amino acid sequences found within SEQ ID No: 1, because claim 53 does not specifically limit the sLTbR to only sequences that comprise SEQ ID No: 1.

The claims recite a "soluble lymphotoxin beta receptor ", heterologous proteins (such as serum albumin, lipoproteins, apolipoproteins, and transferrin), and "a functional sequence of amino acids selected from the amino acids of SEQ ID No: 1" as part of the invention. However, there does not appear to be an adequate written description in the specification as-filed of the essential structural feature that provides coverage for the broad class of sequences or molecules encompassed by the term soluble lymphotoxin beta receptor or functional sequence of amino acids selected from the amino acids of SEQ ID No: 1, because the claims fail to provide for specific functional language that can be correlated to the genus of molecules claimed. Although claim 53 recites a sequence by reference to a SEQ ID number, it does not specifically limit it to only SEQ

ID No: 1, because of the phrase "selected from". The specification has not specifically taught a representative species of which this broad genus of sequence encompasses. Thus one of skill in the art could interpret this as any sequence found within SEQ ID No: 1 (i.e. fragments of sLTβR), none of which have not been disclosed or taught in the specification as filed (*it is noted that is applicant amends the claims to recite a sequence that comprises SEQ ID No: 1, the written description for claim 53 would be overcome). In the case of the heterologous proteins, the specification has only described an immunoglobulin Fc portion conjugated to the sLTβR molecule and therefore, the applicant has not provided sufficient evidence that they were in possession of the invention as claimed.

The Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, ¶ 1 "Written Description" Requirement make clear that the written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species by actual reduction to practice, reduction to drawings, or by disclosure of relevant, identifying characteristics, i.e., structure or other physical and or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the genus (Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001, see especially page 1106 3rd column).

In the instant case, the specification has only provided support for an sLTβR of SEQ ID No: 1, however, the claims encompass any portion of the soluble LTβR or any

fragment of SEQ ID No: 1. With the exception of SEQ ID No: 1, the skilled artisan cannot envision the detailed structure of the encompassed polypeptide or fragments of the polypeptide variants and therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and a reference to a potential method of isolating it. The amino acid sequence itself is required. See *Fiers v. Revel*, 25 USPQ 2d 1601 at 1606 (CAFC 1993) and *Amgen Inc. V. Chugai Pharmaceutical Co. Lts.*, 18 USPQ2d 1016.

With regard to the heterologous proteins, the species of immunoglobulin Fc is not representative of the broad genus of proteins claimed, because the Fc portion does not share or have any core structure that is representative of the broad class of heterologous proteins claimed.

Applicant does not appear to have reduced to practice the broad scope of sLTβR molecules or heterologous proteins claimed. Neither has Applicant provided a sufficient written description of any structure that may be correlated with the desired function of binding to surface LT ligand. A soluble LTβR encompasses *any* sequence found within the extracellular domain of SEQ ID No: 1 with the functional activity of binding to surface LT ligand. Thus the genus of sequences encompassed by this term is extensive and the artisan would not be able to recognize that Applicant was in possession of the invention as now claimed, because the specification has only defined a single sequence, namely SEQ ID No: 1, which represents the entire extracellular domain of LTβR.

Consequently, Applicant was not in possession of the instant claimed invention. See Regents of the University of California v. Eli Lilly and Co. 119 F.3d 1559, 43 USPQ2d 1398 (Fed. Cir. 1997). Adequate written description of genetic material "'requires a precise definition, such as by structure, formula, chemical name, or physical properties,' not a mere wish or plan for obtaining the claimed chemical invention." Id. 43 USPQ2d at 1404 (quoting Fiers, 984 F.2d at 1171, 25 USPQ2d at 1606). The disclosure must allow one skilled in the art to visualize or recognize the identity of the subject matter of the claim. Id. 43 USPQ2d at 1406. A description of what the genetic material does, rather than of what it is, does not suffice. Id.

While it is noted that the instant claims are drawn to methods, the claims nevertheless require an adequate written description of the soluble lymphotoxin beta receptor employed in the methods. Applicant is directed to the Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, ¶ 1 "Written Description" Requirement, Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001. Applicant is invited to point to clear support or specific examples of the claimed invention in the specification as-filed.

Claim Rejections - 35 USC § 112, 1st paragraph

5. Claims 51-58 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to

which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The claims are drawn to a method of treating, preventing or eliminating SLE comprising the administration of a therapeutically effective amount of a soluble lymphotoxin beta receptor (sLTβR). The specification teaches that the administration of an sLTβR containing compound into an imunodeficient SCID mouse and further indicate its ability to inhibit an antibody response (see pages 45 and 63, in particular), however, the specification is devoid of teaching how one of skill in the art is to use the instant method for the treating, prevention or elimination of SLE.

The art teaches that the etiology and mechanism underlying SLE is unknown and is capable of manifesting itself as multiple diseases (see Trethewey P Dimens Crit Care Nurs 2004;23(3):111-115, in particular page 111). It is also known in the art that cures, prevention, or means of eliminating the disease are not yet known, and to date the only means of treating SLE is through the suppression of its symptoms and in the alleviation of any discomfort associated with the disease (see http://reutershealth.com/wellcomnnected/doc63.html, see in particular page 18 -- enclosed). In addition, the art teaches that the typical animal model used to study SLE are conventionally performed in a mouse that has been immunized with a common 16/6 idiotype antibody (Mendlovic *et al* Proc. Natl. Acad. Sci. USA 1988 April;85:2260-2264). Furthermore, it is generally accepted in the art that the prevention of any diseases must be accompanied by quantitative analysis from defined populations which have been successfully pre-screened and are predisposed to particular types of

diseases, and in this case SLE. This type of data might be derived from widespread genetic analysis, gene clusters, or family histories. The essential element towards the validation of a preventive therapeutic is the ability to test the drug on subjects monitored in advance of clinical onset and *link* those results with subsequent histological confirmation of the presence or absence of disease. This irrefutable link between antecedent drug and subsequent knowledge of the prevention of the disease is the essence of a valid preventive agent. Further, a preventive administration also must assume that the therapeutic will be safe and tolerable for anyone susceptible to the disease.

The specification must provide reasonable guidance to one of skill in the art so that the practice of the instant invention may be accomplished without undue experimentation. In the instant case, the specification does not provided one of skill in the art with the necessary information to practice the method to the extent of treating, preventing or eliminating SLE comprising the administration of an sLTβR. The specification has not provided one of skill in the art with any correlation or reasonable expectation of success in treating, preventing or eliminating SLE through the administration of sLTβR based on the disclosure of the specification. As outlined above, the current state of the art teaches that SLE is at most an unpredictable disease, because the onset, the etiology, and the treatment of this disease are not yet fully understood. Because the treatment options for this disease are generally based on alleviating symptoms associated with the disease and because no treatment definitively cures SLE, one of skill in the art would not be capable of practicing the instant invention

without undue experimentation based on the teachings of the instant specification. Furthermore, the specification teaches an atypical or unconventional animal model for the examination of SLE. One of skill in the art would not be accustomed to using the instantly disclosed model for the examination of SLE because as stated above (i.e. Mendlovic *et al*) the conventional or art accepted model of studying SLE utilizes an anti-DNA antibody for the elicitation of induction of the disease. As such, the results outlined and obtained in the instant application utilizing an immunodeficient SCID mouse are unpredictable based on the fact that the skilled artisan would have used the model described by Mendlovic *et al*. Thus one of skill in the art would be forced into undue experimentation to determine if the results obtained using the instantly taught model is predictive or effective as a means to determine treat, prevent, or elimintate SLE.

Therefore, considering large quantity of experimentation needed, the unpredictability of the field, the state of the art, and breadth of the claims, it is concluded that undue experimentation would be required to enable the intended claims. Many of these factors have been summarized *In re Wands, 858 F.2d 731, USPQ2d 1400 (Fed. Cir. 1988).*

Double Patenting

6. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

7. Claims 51-58 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-14 of U.S. Patent Nos. 6,403,087 (herein `087) and 6,669,941 (herein `941). Although the conflicting claims are not identical, they are not patentably distinct from each other because the scope of the claims of the instant invention are encompassed by both `087 and `941 patents.

The claims of the instant invention teach the treatment of SLE comprising the administration of a soluble LTβR. Since the method steps claimed in the instant invention only require a single step, namely the administration of a soluble LTβR, the claims of both `087 and `941 patents anticipate the instantly claimed invention. Furthermore, because it is unclear whether or not SLE is in fact a TH1 or TH2 diseases (as evidenced by Smolen JS Arthritis Research 2002 May; 4(Suppl. 3):S25-S30), for the purposes of this rejection, the SLE diseases claimed in the instant invention fall within the scope of the TH-1 diseases encompassed by both the `087 and `941 patents.

Thus it would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to treat a patient comprising the administration of a sLTβR. because both the `087 and the `941 patents taught the same method steps of administering sLTβR.

Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Christopher H Yaen whose telephone number is 571-272-0838. The examiner can normally be reached on Monday-Friday 9-5.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jeffrey Siew can be reached on 571-272-0787. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

CHY
Art Unit 1642
August 31, 2004

GARY NICKOL
PRIMARY EXAMINER